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July 11, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Docket No. 00N-1262

Dear Sir/Madam:

This responds to the Federal Register notice of May 5, 2000 requesting comments on "Improving Premarket Review and Approval of Food and Color Additives in the Center for Food Safety and Applied Nutrition". This response is divided into three segments including a predictable review process, the Institute of Medicine's Workshop, and FDA's questions.

Over the course of the last ten years, ARCO Chemical Company and the successor company, Lyondell Chemical Company, have sought partners to commercialize a novel technology based on esterified propoxylated glycerol ("EPG"). The EPG technology is being spun-out to a new start-up company named Viritech Inc. staffed by former employees and consultants.

EPG is an extended triglyceride whose major use is as a 1-for-1 fat substitute for conventional dietary fats and oils. A Master File has been established at FDA for EPG. Pivotal pre-clinical and clinical studies have been successfully completed. We anticipate submitting a food additive petition to the Center for Food Safety and Applied Nutrition requesting approval of EPG.

A Predictable Review Process

During the partner search, we learned that food companies have a short-term focus, measured in quarters, which precludes their participation as long-term partners in a long-term development. Pharmaceutical companies have the necessary longer-term perspective, measured in years, appropriate for development of a macro-nutrient food additive petition. However, pharmaceutical companies typically invest their research dollars in what are deemed more profitable pharmaceutical products. When you delve

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into the economic aspects of successful food additives such as aspartame you realize that sales of one billion dollars per year are possible with major food ingredients. On closer analysis, the decision to proceed with a major food additive or an equally profitable pharmaceutical frequently relies on an analysis of the risk encountered during the regulatory review period at CFSAN or CDER. Review of new drug applications has improved substantially in recent years to the point that review times at FDA's CDER are now reasonably predictable. By contrast, review periods for food additives with CFSAN are not predictable. Investors have options. Today, investing in a new company pursuing a food additive petition carries far more regulatory review risk than a similar investment in a company pursuing a new pharmaceutical or medical device.

Removing the uncertainty from the FDA review process is an important issue for large, well-funded companies. Delay, the companion to a process that is not predictable, translates into lost revenue on the income side while spending continues on the expense side of the ledger. From a consumer perspective, the benefits resulting from the new approval are delayed and effectively denied.

For a small company, dependent on capital markets for new dollars to sustain the company, a non-predictable process translates into more expensive dollars. When delay creeps into the regulatory review, investors are reluctant to add new capital that is deemed at immediate risk due to the uncertain review process. The survival of the small company encountering delay is in jeopardy.

Institute of Medicine's Workshop

The Institute of Medicine's 1997 workshop titled "Enhancing the Regulatory Decision-Making Approval Process for Direct Food Ingredient Technologies" and the Workshop Summary bear directly on the subject of improving pre-market review and approval of food and color additives. (Enhancing the Regulatory Decision-Making Approval Process for Direct Food Ingredient Technologies, 1999, National Academy Press) Three paragraphs from pages 1 and 2 of the Workshop Summary are reproduced below:

> Three major themes emerged during the workshop. First, communication is a key to enhancing the regulatory review process. Well-developed food additive petitions that include all of the necessary data can only serve to enhance

scarce agency resources. However, the determination of the appropriate level of communication needs further exploration. What some may consider to be a consultative process may appear to be collaborative to others.

Second, solving complex food ingredient issues requires the involvement of many scientific disciplines that are often not available within the FDA staff. Often, outside experts residing in academia, professional scientific associations, and public interest groups may need to be involved in the evaluation process, but barriers, such as the Federal Advisory Committee Act and the confidential nature of the data submitted, limit the involvement of outside experts.

Finally, the possibility of congressional authorization of user fees to enhance FDA's diminishing resources needs further discussion. Many participants agreed with the user fee concept, but representatives of the public interest groups were opposed to the idea of manufacturers paying for FDA contractor-approved petition reviews. Manufacturers are reluctant to pay a user fee without some assurance of benefit, such as market exclusivity. Continued exploration of the fundamental public policy issues raised by user fees is critical to mutual understanding among all parties.

We agree that these three paragraphs frame the core of the discussion on how to improve pre-market review and approval. Each of these issues is further considered here.

Communications: We favor improved communications between petitioners and FDA. While the Center is sometimes reluctant to engage in intensive discussions prior to submission and acceptance of the formal petition, this pre-petition period offers the best opportunity to improve the predictability of the formal review process. If both parties can come to mutual understanding on the planned exposure from the new food additive, the completed content of the petition, and petition gaps, the petitioner can go forward with planning and budgeting for new studies with a degree of confidence.

In the industrial community, there are always competing requests for research and development dollars. Understanding FDA's point of view on the need for new studies permits corporate management to sift through the competitive requests and place emphasis on those projects with the brightest prospects and shortest timelines. The budgetary constraints in a small company are acute. The small company does not have the resources to repeat

pivotal studies. The design and execution must be right the first time. Reaching agreement with FDA on protocol design is only possible after open and candid discussion with the petitioner.

Outside FDA Experts: We favor and encourage FDA to draw upon the talents of experts outside the Center, and outside of FDA to resolve complex scientific issues. The Center successfully used the talents of outside experts to resolve difficult issues inherent in the olestra petition. We favor the use of experts in (a) pending petitions and (b) those new petitions that will come to the Agency in the future. Outside experts can improve the predictability of petition reviews. A single knotty issue, new to the Center, can stymie a petition for months or years. A single expert or panel of experts has the intellectual power to cut through the knot and help the Center reach resolution. We do not see the confidential nature of the data submitted in the food additive petition as a major obstacle to the use of outside experts.

User Fees: We support the concept of fees for review of food additive petitions <u>if</u> the fees are tied to a predictable schedule for petition review. We do not support FDA contractor-approved petition reviews. The public has a right to know who reviewed and approved a food additive petition. When a third party reviews the petition, the expected uniformity and expected fairness of review from one petition to the next may be lost.

FDA's Questions

Question 1. The Federal Register notice asked for "What specific changes can be made to make the current review process more efficient, i.e., transparent, timely, responsive, and predictable, while preserving these high standards of data review and safety?" In thinking about this request, we focused on predictable as a transcending issue which encompasses the concepts of timely and responsive. Timely, responsive and predictable are all terms that relate to the process and the eventual decision rendered by the Center.

Transparent has many aspects, transparent to the petitioner, to competitors, to consumer groups, to public health groups, to the scientific community, to the public at large, and to others. Representing the interests of the petitioner, we prefer that the process and status of the petition be transparent to the

petitioner. In the absence of a transparent process, uncertainty and antagonism between the petitioner and the Center can result. Good communication coupled with a transparent process form the basis for rapid progress to a regulatory decision. Because each petition will contain a limited amount of information that is confidential, and hence not available under the Freedom of Information Act, the petition process can not and should not be equally transparent to all interested parties. Competitors, seeking to protect their market positions, have perfected the practice of raising issues with the Center during the deliberative process. This process is described by Lars Noah and summarized in the "Legal Aspects of the Food Additive Approval Process" (Institute of Medicine, Workshop Summary of Enhancing the Regulatory Decision-Making Process for Direct Food Ingredient Technologies", National Academy Press, 1999). These are disruptive to FDA's review process. We support the still pending Citizen's Petition authored by Peter Barton Hutt in 1992 that provided a roadmap to deal with such comments.

Question 2. Setting priorities on one class of food additive petition over all other classes runs counter to our goal of a predictable review process. We favor no priorities. Alternatively, we favor a broader priority for food additive petitions whose approval has significant public health benefits. In the later case, the petitioner would have the burden of establishing the case for a significant public health benefit from approval of the petitioned food additive to establish a priority review.

Questions 3 and 4. We support (1) performing prefiling consultations with prospective applicants for new food additives and for new uses for previously approved food additives, and (2) adding personnel resources to the review process. We believe that emphasis in both of these areas will produce measurable, significant improvements in the review and approval of food and color additives. We are not confident that (3) enhancing electronic data management systems such as automated workflow management or data warehousing will lead to the desired predictable review process. We find the suggestion of (4) acquiring or monitoring new safety information on already approved additives is not an activity that directly contributes to a predictable review process and hence is a lower priority.

We appreciate this opportunity to contribute to the record. From a small company prospective, altering the regulatory process to eliminate delay and inserting a predictable regulatory review is vital to obtaining investor funding. Indeed, unless the process

is altered, the submission of new food additive petitions will wither in face of alternative opportunities for investment. The capital markets, the source of funding for small companies, are unforgiving and quick to punish those who break their timeline commitments. The Center has the responsibility, opportunity and funding to improve its review and approval of food and color additive petitions.

Respectively submitted,

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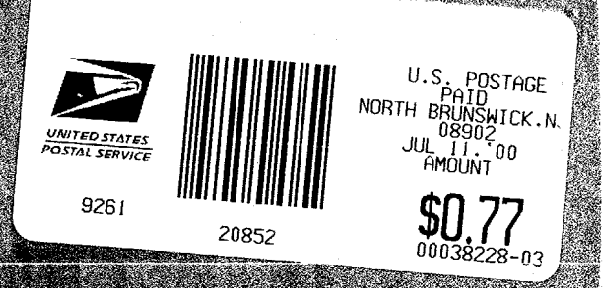

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